```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:00:49 ON 04 JUN 2001

=> fil .bec
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         1.05       1.05

FILE 'BIOTECHDS' ACCESS NOT AUTHORIZED
FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE,
       BIOTECHNO' ENTERED AT 15:04:46 ON 04 JUN 2001
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

9 FILES IN THE FILE LIST

=> s carbon(2a)(flux or flow)
FILE 'MEDLINE'
        171519 CARBON
         18713 FLUX
        269049 FLOW
L1         551 CARBON(2A)(FLUX OR FLOW)

FILE 'SCISEARCH'
        245718 CARBON
         94345 FLUX
        422938 FLOW
L2        2073 CARBON(2A)(FLUX OR FLOW)

FILE 'LIFESCI'
         37332 CARBON
          8505 FLUX
         38517 FLOW
L3         798 CARBON(2A)(FLUX OR FLOW)

FILE 'BIOSIS'
        209917 CARBON
         37753 FLUX
        290132 FLOW
L4        2555 CARBON(2A)(FLUX OR FLOW)

FILE 'EMBASE'
        114261 CARBON
         22295 FLUX
        281693 FLOW
L5         686 CARBON(2A)(FLUX OR FLOW)

FILE 'HCAPLUS'
        813797 CARBON
        189873 FLUX
        601368 FLOW
L6        3966 CARBON(2A)(FLUX OR FLOW)

FILE 'NTIS'
         67773 CARBON
         35117 FLUX
        158571 FLOW
L7         244 CARBON(2A)(FLUX OR FLOW)
```

```
FILE 'ESBIOBASE'
         37759 CARBON
         10549 FLUX
         57729 FLOW
L8         691 CARBON(2A)(FLUX OR FLOW)

FILE 'BIOTECHNO'
         28206 CARBON
          5733 FLUX
         39068 FLOW
L9         403 CARBON(2A)(FLUX OR FLOW)

TOTAL FOR ALL FILES
L10      11967 CARBON(2A)(FLUX OR FLOW)

=> s l11(6a)(modif? or alter? or increas?)
FILE 'MEDLINE'
L11 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l10(6a)(modif? or alter? or increas?)
FILE 'MEDLINE'
        266133 MODIF?
        492766 ALTER?
       1464541 INCREAS?
L11         65 L1 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'SCISEARCH'
        348287 MODIF?
        457622 ALTER?
       1361552 INCREAS?
L12        134 L2 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'LIFESCI'
         74001 MODIF?
        135323 ALTER?
        385560 INCREAS?
L13         73 L3 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'BIOSIS'
        294942 MODIF?
        902484 ALTER?
       1664439 INCREAS?
L14        156 L4 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'EMBASE'
        257055 MODIF?
        480808 ALTER?
       1445943 INCREAS?
L15         74 L5 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'HCAPLUS'
        687933 MODIF?
        629153 ALTER?
       3019774 INCREAS?
L16        161 L6 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'NTIS'
```

```
         92330 MODIF?
         84850 ALTER?
        169153 INCREAS?
L17          9 L7 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'ESBIOBASE'
         85190 MODIF?
        136673 ALTER?
        412907 INCREAS?
L18         64 L8 (6A)(MODIF? OR ALTER? OR INCREAS?)

FILE 'BIOTECHNO'
         66989 MODIF?
        116480 ALTER?
        301878 INCREAS?
L19         47 L9 (6A)(MODIF? OR ALTER? OR INCREAS?)

TOTAL FOR ALL FILES
L20        783 L10(6A)(MODIF? OR ALTER? OR INCREAS?)  24

=> s (phosphoenolpyruvate or (phospho enol or phosphoenol)(w)pyruvate or
pep)(4a)(suppl#### or availab?)
FILE 'MEDLINE'
          5737 PHOSPHOENOLPYRUVATE
          2769 PHOSPHO
           656 ENOL
            58 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           212 PHOSPHOENOL
         21650 PYRUVATE
          2592 PEP
        293413 SUPPL####
        224871 AVAILAB?
L21         32 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'SCISEARCH'
          5125 PHOSPHOENOLPYRUVATE
          2267 PHOSPHO
          6137 ENOL
            61 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           198 PHOSPHOENOL
         16234 PYRUVATE
          2294 PEP
         86550 SUPPL####
        253392 AVAILAB?
L22         38 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'LIFESCI'
          1901 PHOSPHOENOLPYRUVATE
          1043 "PHOSPHO"
           218 "ENOL"
            20 PHOSPHO ENOL
                 ("PHOSPHO"(W)"ENOL")
           106 PHOSPHOENOL
          5196 PYRUVATE
           777 PEP
```

```
         18178 SUPPL####
         68484 AVAILAB?
L23         19 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'BIOSIS'
          6991 PHOSPHOENOLPYRUVATE
         55595 PHOSPHO
          1886 ENOL
           151 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
          3610 PHOSPHOENOL
         32624 PYRUVATE
          3410 PEP
         88435 SUPPL####
        223224 AVAILAB?
L24         38 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'EMBASE'
          3928 PHOSPHOENOLPYRUVATE
          2133 "PHOSPHO"
          1554 "ENOL"
            40 PHOSPHO ENOL
                 ("PHOSPHO"(W)"ENOL")
           164 PHOSPHOENOL
         17892 PYRUVATE
          2371 PEP
         65475 SUPPL####
        224916 AVAILAB?
L25         30 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'HCAPLUS'
          9920 PHOSPHOENOLPYRUVATE
          6926 PHOSPHO
         17787 ENOL
            52 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           551 PHOSPHOENOL
         43337 PYRUVATE
          5153 PEP
        182395 SUPPL####
        316742 AVAILAB?
L26         60 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'NTIS'
            36 PHOSPHOENOLPYRUVATE
            48 PHOSPHO
            74 ENOL
             0 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
             5 PHOSPHOENOL
           299 PYRUVATE
          1164 PEP
         83018 SUPPL####
        233348 AVAILAB?
L27         16 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
```

```
                OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'ESBIOBASE'
          1402 PHOSPHOENOLPYRUVATE
          1062 PHOSPHO
           299 ENOL
            22 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
            55 PHOSPHOENOL
          4190 PYRUVATE
           684 PEP
         17201 SUPPL####
         62856 AVAILAB?
L28         12 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

FILE 'BIOTECHNO'
          2120 PHOSPHOENOLPYRUVATE
          1124 PHOSPHO
           152 ENOL
            17 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
            65 PHOSPHOENOL
          5526 PYRUVATE
           657 PEP
         10810 SUPPL####
         43572 AVAILAB?
L29         15 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
               OR PEP)(4A)(SUPPL#### OR AVAILAB?)

TOTAL FOR ALL FILES
L30        260 (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W) PYRUVAT
               E OR PEP)(4A)(SUPPL#### OR AVAILAB?)

=> s phosphotransferase# or phospho transferase#
FILE 'MEDLINE'
         17633 PHOSPHOTRANSFERASE#
          2769 PHOSPHO
         36615 TRANSFERASE#
            14 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L31      17641 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'SCISEARCH'
          4037 PHOSPHOTRANSFERASE#
          2267 PHOSPHO
         30525 TRANSFERASE#
            13 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L32       4048 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'LIFESCI'
          2504 PHOSPHOTRANSFERASE#
          1043 "PHOSPHO"
         10529 TRANSFERASE#
             7 PHOSPHO TRANSFERASE#
                 ("PHOSPHO"(W)TRANSFERASE#)
L33       2508 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#
```

```
FILE 'BIOSIS'
          5521 PHOSPHOTRANSFERASE#
         55595 PHOSPHO
         62006 TRANSFERASE#
          1751 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L34       6624 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'EMBASE'
          7822 PHOSPHOTRANSFERASE#
          2133 "PHOSPHO"
         28159 TRANSFERASE#
             6 PHOSPHO TRANSFERASE#
                 ("PHOSPHO"(W)TRANSFERASE#)
L35       7827 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'HCAPLUS'
          6754 PHOSPHOTRANSFERASE#
          6926 PHOSPHO
         36938 TRANSFERASE#
            12 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L36       6763 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'NTIS'
           126 PHOSPHOTRANSFERASE#
            48 PHOSPHO
           828 TRANSFERASE#
             0 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L37         126 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'ESBIOBASE'
          2733 PHOSPHOTRANSFERASE#
          1062 PHOSPHO
         21681 TRANSFERASE#
             5 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L38       2736 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

FILE 'BIOTECHNO'
          5133 PHOSPHOTRANSFERASE#
          1124 PHOSPHO
         12894 TRANSFERASE#
             4 PHOSPHO TRANSFERASE#
                 (PHOSPHO(W)TRANSFERASE#)
L39       5135 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE#

TOTAL FOR ALL FILES
L40      53408 PHOSPHOTRANSFERASE# OR PHOSPHO TRANSFERASE# 60

=> s l40 and l10
FILE 'MEDLINE'
L41         15 L31 AND L1

FILE 'SCISEARCH'
L42         21 L32 AND L2

FILE 'LIFESCI'
```

```
L43           7 L33 AND L3

FILE 'BIOSIS'
L44          11 L34 AND L4

FILE 'EMBASE'
L45           8 L35 AND L5

FILE 'HCAPLUS'
L46          13 L36 AND L6

FILE 'NTIS'
L47           1 L37 AND L7

FILE 'ESBIOBASE'
L48           8 L38 AND L8

FILE 'BIOTECHNO'
L49           8 L39 AND L9

TOTAL FOR ALL FILES
L50          92 L40 AND L10   72

=> s l40(8a)(delet? or inactivat?)
FILE 'MEDLINE'
         95846 DELET?
         82661 INACTIVAT?
L51        106 L31(8A)(DELET? OR INACTIVAT?)

FILE 'SCISEARCH'
         80518 DELET?
         64898 INACTIVAT?
L52         49 L32(8A)(DELET? OR INACTIVAT?)

FILE 'LIFESCI'
         44122 DELET?
         31546 INACTIVAT?
L53         63 L33(8A)(DELET? OR INACTIVAT?)

FILE 'BIOSIS'
         92102 DELET?
         91024 INACTIVAT?
L54        111 L34(8A)(DELET? OR INACTIVAT?)

FILE 'EMBASE'
         81290 DELET?
         72634 INACTIVAT?
L55         74 L35(8A)(DELET? OR INACTIVAT?)

FILE 'HCAPLUS'
         90060 DELET?
        114553 INACTIVAT?
L56        143 L36(8A)(DELET? OR INACTIVAT?)

FILE 'NTIS'
          4131 DELET?
          1965 INACTIVAT?
L57          0 L37(8A)(DELET? OR INACTIVAT?)
```

```
FILE 'ESBIOBASE'
         39036 DELET?
         25310 INACTIVAT?
L58         17 L38(8A)(DELET? OR INACTIVAT?)

FILE 'BIOTECHNO'
         58184 DELET?
         32463 INACTIVAT?
L59         47 L39(8A)(DELET? OR INACTIVAT?)

TOTAL FOR ALL FILES
L60        610 L40(8A)(DELET? OR INACTIVAT?)  84

=> s l60 and transport?
FILE 'MEDLINE'
        212221 TRANSPORT?
L61          9 L51 AND TRANSPORT?

FILE 'SCISEARCH'
        312532 TRANSPORT?
L62          1 L52 AND TRANSPORT?

FILE 'LIFESCI'
         57930 TRANSPORT?
L63          2 L53 AND TRANSPORT?

FILE 'BIOSIS'
        930642 TRANSPORT?
L64         11 L54 AND TRANSPORT?

FILE 'EMBASE'
        218793 TRANSPORT?
L65          9 L55 AND TRANSPORT?

FILE 'HCAPLUS'
        544509 TRANSPORT?
L66         16 L56 AND TRANSPORT?

FILE 'NTIS'
        129529 TRANSPORT?
L67          0 L57 AND TRANSPORT?

FILE 'ESBIOBASE'
        127906 TRANSPORT?
L68          1 L58 AND TRANSPORT?

FILE 'BIOTECHNO'
         63819 TRANSPORT?
L69          3 L59 AND TRANSPORT?

TOTAL FOR ALL FILES
L70         52 L60 AND TRANSPORT?     96

=> s l40 and glucose
FILE 'MEDLINE'
        218960 GLUCOSE
L71       2227 L31 AND GLUCOSE

FILE 'SCISEARCH'
```

```
        141907 GLUCOSE
L72        740 L32 AND GLUCOSE

FILE 'LIFESCI'
         35148 GLUCOSE
L73        458 L33 AND GLUCOSE

FILE 'BIOSIS'
        228090 GLUCOSE
L74       1104 L34 AND GLUCOSE

FILE 'EMBASE'
        178908 GLUCOSE
L75        905 L35 AND GLUCOSE

FILE 'HCAPLUS'
        304062 GLUCOSE
L76       1289 L36 AND GLUCOSE

FILE 'NTIS'
          2794 GLUCOSE
L77          9 L37 AND GLUCOSE

FILE 'ESBIOBASE'
         38663 GLUCOSE
L78        382 L38 AND GLUCOSE

FILE 'BIOTECHNO'
         34995 GLUCOSE
L79        563 L39 AND GLUCOSE

TOTAL FOR ALL FILES
L80       7677 L40 AND GLUCOSE    158

=> s l60 and l80
FILE 'MEDLINE'
L81          16 L51 AND L71

FILE 'SCISEARCH'
L82           4 L52 AND L72

FILE 'LIFESCI'
L83           6 L53 AND L73

FILE 'BIOSIS'
L84          16 L54 AND L74

FILE 'EMBASE'
L85          14 L55 AND L75

FILE 'HCAPLUS'
L86          20 L56 AND L76

FILE 'NTIS'
L87           0 L57 AND L77

FILE 'ESBIOBASE'
L88           3 L58 AND L78
```

```
FILE 'BIOTECHNO'
L89           7 L59 AND L79

TOTAL FOR ALL FILES
L90          86 L60 AND L80                    120

=> s l80 and transport
FILE 'MEDLINE'
        178166 TRANSPORT
L91        608 L71 AND TRANSPORT

FILE 'SCISEARCH'
        275484 TRANSPORT
L92        329 L72 AND TRANSPORT

FILE 'LIFESCI'
         46564 TRANSPORT
L93        184 L73 AND TRANSPORT

FILE 'BIOSIS'
        899753 TRANSPORT
L94        372 L74 AND TRANSPORT

FILE 'EMBASE'
        197806 TRANSPORT
L95        401 L75 AND TRANSPORT

FILE 'HCAPLUS'
        489058 TRANSPORT
L96        513 L76 AND TRANSPORT

FILE 'NTIS'
         75037 TRANSPORT
L97          3 L77 AND TRANSPORT

FILE 'ESBIOBASE'
        118821 TRANSPORT
L98        186 L78 AND TRANSPORT

FILE 'BIOTECHNO'
         56295 TRANSPORT
L99        270 L79 AND TRANSPORT

TOTAL FOR ALL FILES
L100      2866 L80 AND TRANSPORT                132

=> s l100 and (phosphoenolpyruvate or (phospho enol or phosphoenol)(w)pyruvate or
pep)
FILE 'MEDLINE'
          5737 PHOSPHOENOLPYRUVATE
          2769 PHOSPHO
           656 ENOL
            58 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           212 PHOSPHOENOL
         21650 PYRUVATE
           238 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          2592 PEP
L101       326 L91 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
```

```
                PYRUVATE OR PEP)

FILE 'SCISEARCH'
          5125 PHOSPHOENOLPYRUVATE
          2267 PHOSPHO
          6137 ENOL
            61 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           198 PHOSPHOENOL
         16234 PYRUVATE
           242 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          2294 PEP
L102       227 L92 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'LIFESCI'
          1901 PHOSPHOENOLPYRUVATE
          1043 "PHOSPHO"
           218 "ENOL"
            20 PHOSPHO ENOL
                 ("PHOSPHO"(W)"ENOL")
           106 PHOSPHOENOL
          5196 PYRUVATE
           116 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
           777 PEP
L103       134 L93 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'BIOSIS'
          6991 PHOSPHOENOLPYRUVATE
         55595 PHOSPHO
          1886 ENOL
           151 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
          3610 PHOSPHOENOL
         32624 PYRUVATE
          3699 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          3410 PEP
L104       251 L94 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'EMBASE'
          3928 PHOSPHOENOLPYRUVATE
          2133 "PHOSPHO"
          1554 "ENOL"
            40 PHOSPHO ENOL
                 ("PHOSPHO"(W)"ENOL")
           164 PHOSPHOENOL
         17892 PYRUVATE
           187 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          2371 PEP
L105       251 L95 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'HCAPLUS'
          9920 PHOSPHOENOLPYRUVATE
          6926 PHOSPHO
         17787 ENOL
            52 PHOSPHO ENOL
```

```
                (PHOSPHO(W)ENOL)
          551 PHOSPHOENOL
        43337 PYRUVATE
          526 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
         5153 PEP
L106      381 L96 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
              PYRUVATE OR PEP)

FILE 'NTIS'
           36 PHOSPHOENOLPYRUVATE
           48 PHOSPHO
           74 ENOL
            0 PHOSPHO ENOL
                (PHOSPHO(W)ENOL)
            5 PHOSPHOENOL
          299 PYRUVATE
            3 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
         1164 PEP
L107        3 L97 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
              PYRUVATE OR PEP)

FILE 'ESBIOBASE'
         1402 PHOSPHOENOLPYRUVATE
         1062 PHOSPHO
          299 ENOL
           22 PHOSPHO ENOL
                (PHOSPHO(W)ENOL)
           55 PHOSPHOENOL
         4190 PYRUVATE
           75 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          684 PEP
L108       98 L98 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
              PYRUVATE OR PEP)

FILE 'BIOTECHNO'
         2120 PHOSPHOENOLPYRUVATE
         1124 PHOSPHO
          152 ENOL
           17 PHOSPHO ENOL
                (PHOSPHO(W)ENOL)
           65 PHOSPHOENOL
         5526 PYRUVATE
           76 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          657 PEP
L109      171 L99 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
              PYRUVATE OR PEP)

TOTAL FOR ALL FILES
L110     1842 L100 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W 144
              ) PYRUVATE OR PEP)

=> s l110 and mut/q
FILE 'MEDLINE'
L111      205 L101 AND MUT/Q

FILE 'SCISEARCH'
L112      134 L102 AND MUT/Q

FILE 'LIFESCI'
```

```
L113         69 L103 AND MUT/Q

FILE 'BIOSIS'
L114        139 L104 AND MUT/Q

FILE 'EMBASE'
L115        139 L105 AND MUT/Q

FILE 'HCAPLUS'
L116        200 L106 AND MUT/Q

FILE 'NTIS'
L117          2 L107 AND MUT/Q

FILE 'ESBIOBASE'
L118         62 L108 AND MUT/Q

FILE 'BIOTECHNO'
L119        101 L109 AND MUT/Q

TOTAL FOR ALL FILES
L120       1051 L110 AND MUT/Q     156

=> s l120 and (aromatic or shikimate)
FILE 'MEDLINE'
         21820 AROMATIC
           302 SHIKIMATE
L121         2 L111 AND (AROMATIC OR SHIKIMATE)

FILE 'SCISEARCH'
         73889 AROMATIC
           689 SHIKIMATE
L122         3 L112 AND (AROMATIC OR SHIKIMATE)

FILE 'LIFESCI'
         11409 AROMATIC
           236 SHIKIMATE
L123         2 L113 AND (AROMATIC OR SHIKIMATE)

FILE 'BIOSIS'
         39555 AROMATIC
          1004 SHIKIMATE
L124         2 L114 AND (AROMATIC OR SHIKIMATE)

FILE 'EMBASE'
         35600 AROMATIC
           262 SHIKIMATE
L125         2 L115 AND (AROMATIC OR SHIKIMATE)

FILE 'HCAPLUS'
        173305 AROMATIC
        235312 AROM
        326665 AROMATIC
                 (AROMATIC OR AROM)
          1518 SHIKIMATE
L126         5 L116 AND (AROMATIC OR SHIKIMATE)

FILE 'NTIS'
         11111 AROMATIC
```

```
             8 SHIKIMATE
L127         0 L117 AND (AROMATIC OR SHIKIMATE)

FILE 'ESBIOBASE'
         10653 AROMATIC
           202 SHIKIMATE
L128         1 L118 AND (AROMATIC OR SHIKIMATE)

FILE 'BIOTECHNO'
         10059 AROMATIC
           179 SHIKIMATE
L129         2 L119 AND (AROMATIC OR SHIKIMATE)

TOTAL FOR ALL FILES
L130        19 L120 AND (AROMATIC OR SHIKIMATE)  168

=> s l20 and (phosphoenolpyruvate or (phospho enol or phosphoenol)(w)pyruvate or
pep)
FILE 'MEDLINE'
          5737 PHOSPHOENOLPYRUVATE
          2769 PHOSPHO
           656 ENOL
            58 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           212 PHOSPHOENOL
         21650 PYRUVATE
           238 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          2592 PEP
L131         6 L11 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'SCISEARCH'
          5125 PHOSPHOENOLPYRUVATE
          2267 PHOSPHO
          6137 ENOL
            61 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           198 PHOSPHOENOL
         16234 PYRUVATE
           242 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          2294 PEP
L132         9 L12 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'LIFESCI'
          1901 PHOSPHOENOLPYRUVATE
          1043 "PHOSPHO"
           218 "ENOL"
            20 PHOSPHO ENOL
                 ("PHOSPHO"(W)"ENOL")
           106 PHOSPHOENOL
          5196 PYRUVATE
           116 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
           777 PEP
L133         8 L13 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'BIOSIS'
          6991 PHOSPHOENOLPYRUVATE
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         55595 PHOSPHO
          1886 ENOL
           151 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
          3610 PHOSPHOENOL
         32624 PYRUVATE
          3699 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          3410 PEP
L134        15 L14 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'EMBASE'
          3928 PHOSPHOENOLPYRUVATE
          2133 "PHOSPHO"
          1554 "ENOL"
            40 PHOSPHO ENOL
                 ("PHOSPHO"(W)"ENOL")
           164 PHOSPHOENOL
         17892 PYRUVATE
           187 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          2371 PEP
L135         6 L15 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'HCAPLUS'
          9920 PHOSPHOENOLPYRUVATE
          6926 PHOSPHO
         17787 ENOL
            52 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
           551 PHOSPHOENOL
         43337 PYRUVATE
           526 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          5153 PEP
L136        18 L16 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'NTIS'
            36 PHOSPHOENOLPYRUVATE
            48 PHOSPHO
            74 ENOL
             0 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
             5 PHOSPHOENOL
           299 PYRUVATE
             3 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          1164 PEP
L137         0 L17 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
               PYRUVATE OR PEP)

FILE 'ESBIOBASE'
          1402 PHOSPHOENOLPYRUVATE
          1062 PHOSPHO
           299 ENOL
            22 PHOSPHO ENOL
                 (PHOSPHO(W)ENOL)
            55 PHOSPHOENOL
          4190 PYRUVATE
            75 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
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          684 PEP
L138        6 L18 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
              PYRUVATE OR PEP)

FILE 'BIOTECHNO'
         2120 PHOSPHOENOLPYRUVATE
         1124 PHOSPHO
          152 ENOL
           17 PHOSPHO ENOL
                (PHOSPHO(W)ENOL)
           65 PHOSPHOENOL
         5526 PYRUVATE
           76 (PHOSPHO ENOL OR PHOSPHOENOL)(W)PYRUVATE
          657 PEP
L139        6 L19 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)
              PYRUVATE OR PEP)

TOTAL FOR ALL FILES
L140       74 L20 AND (PHOSPHOENOLPYRUVATE OR (PHOSPHO ENOL OR PHOSPHOENOL)(W)  180
               PYRUVATE OR PEP)

=> s l20 and glucose
FILE 'MEDLINE'
       218960 GLUCOSE
L141       24 L11 AND GLUCOSE

FILE 'SCISEARCH'
       141907 GLUCOSE
L142       26 L12 AND GLUCOSE

FILE 'LIFESCI'
        35148 GLUCOSE
L143       15 L13 AND GLUCOSE

FILE 'BIOSIS'
       228090 GLUCOSE
L144       33 L14 AND GLUCOSE

FILE 'EMBASE'
       178908 GLUCOSE
L145       30 L15 AND GLUCOSE

FILE 'HCAPLUS'
       304062 GLUCOSE
L146       33 L16 AND GLUCOSE

FILE 'NTIS'
         2794 GLUCOSE
L147        0 L17 AND GLUCOSE

FILE 'ESBIOBASE'
        38663 GLUCOSE
L148       16 L18 AND GLUCOSE

FILE 'BIOTECHNO'
        34995 GLUCOSE
L149       21 L19 AND GLUCOSE        142

TOTAL FOR ALL FILES
```

```
L150       198 L20 AND GLUCOSE

=> s (l30 or l50 or l70 or l90 or l120 or l130 or l140 or l150) and py=<1995
range=2000,
FILE 'MEDLINE'
          2803 PY=<1995
L151         0 (L21 OR L41 OR L61 OR L81 OR L111 OR L121 OR L131 OR L141) AND
               PY=<1995

FILE 'SCISEARCH'
             0 PY=<1995
L152         0 (L22 OR L42 OR L62 OR L82 OR L112 OR L122 OR L132 OR L142) AND
               PY=<1995

FILE 'LIFESCI'
           191 PY=<1995
L153         0 (L23 OR L43 OR L63 OR L83 OR L113 OR L123 OR L133 OR L143) AND
               PY=<1995

FILE 'BIOSIS'
            35 PY=<1995
L154         0 (L24 OR L44 OR L64 OR L84 OR L114 OR L124 OR L134 OR L144) AND
               PY=<1995

FILE 'EMBASE'
             0 PY=<1995
L155         0 (L25 OR L45 OR L65 OR L85 OR L115 OR L125 OR L135 OR L145) AND
               PY=<1995

FILE 'HCAPLUS'
          3266 PY=<1995
L156         0 (L26 OR L46 OR L66 OR L86 OR L116 OR L126 OR L136 OR L146) AND
               PY=<1995

FILE 'NTIS'
          8472 PY=<1995
L157         0 (L27 OR L47 OR L67 OR L87 OR L117 OR L127 OR L137 OR L147) AND
               PY=<1995

FILE 'ESBIOBASE'
             0 PY=<1995
L158         0 (L28 OR L48 OR L68 OR L88 OR L118 OR L128 OR L138 OR L148) AND
               PY=<1995

FILE 'BIOTECHNO'
        845083 PY=<1995
L159        75 (L29 OR L49 OR L69 OR L89 OR L119 OR L129 OR L139 OR L149) AND
               PY=<1995

TOTAL FOR ALL FILES
L160        75 (L30 OR L50 OR L70 OR L90 OR L120 OR L130 OR L140 OR L150) AND
               PY=<1995

=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              23.20      24.25

STN INTERNATIONAL LOGOFF AT 15:19:00 ON 04 JUN 2001
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	L #	Hits	Search Text	DBs	Time Stamp
1	L1	3000	carbon near2 (flux or flow)	USPAT; US-PGPUB	2001/06/04 15:26
2	L2	150	1 near4 (modif$8 or alter$8 or increas$8)	USPAT; US-PGPUB	2001/06/04 15:27
3	L3	104	(phosphoenol adj pyruvate or pep or phosphoenolpyruvate or phospho adj enol adj pyruvate) near4 (suppl$4 or availab$8)	USPAT; US-PGPUB	2001/06/04 15:28
4	L4	2	2 and 3	USPAT; US-PGPUB	2001/06/04 15:29
5	L5	2505	phosphotransferase$1 or phospho adj transferase$1	USPAT; US-PGPUB	2001/06/04 15:28
6	L6	8	(2 or 3) and 5	USPAT; US-PGPUB	2001/06/04 15:29
7	L7	19	(2 or 3) same (aromatic or shikimate)	USPAT; US-PGPUB	2001/06/04 15:31

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	3000	carbon near2 (flux or flow)	USPAT; US-PGPUB	2001/06/04 15:26
2	L2	150	1 near4 (modif$8 or alter$8 or increas$8)	USPAT; US-PGPUB	2001/06/04 15:27
3	L3	104	(phosphoenol adj pyruvate or pep or phosphoenolpyruvate or phospho adj enol adj pyruvate) near4 (suppl$4 or availab$8)	USPAT; US-PGPUB	2001/06/04 15:28
4	L4	2	2 and 3	USPAT; US-PGPUB	2001/06/04 15:29
5	L5	2505	phosphotransferase$1 or phospho adj transferase$1	USPAT; US-PGPUB	2001/06/04 15:28
6	L6	8	(2 or 3) and 5	USPAT; US-PGPUB	2001/06/04 15:29

US-CL-CURRENT: 435/252.3,435/419 ,435/485 ,435/486 ,435/487 ,435/488 ,435/69.1 ,536/23.1 ,536/23.2 ,536/23.6

US-PAT-NO: 6204063
DOCUMENT-IDENTIFIER: US 6204063 B1
TITLE: Plant glycolysis and respiration enzymes
DATE-ISSUED: March 20, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Allen; Stephen M.	Wilmington	DE	N/A	N/A
Lee; Jian-Ming	Wilmington	DE	N/A	N/A
Lightner; Jonathan E.	Airville	PA	N/A	N/A
Odell; Joan T.	Unionville	PA	N/A	N/A

US-CL-CURRENT: 435/468,435/252.3 ,435/419 ,435/485 ,435/486 ,435/487 ,435/488 ,435/69.1 ,536/23.1 ,536/23.2 ,536/23.6
ABSTRACT:

This invention relates to an isolated nucleic acid fragment encoding a glycolysis or respiration protein. The invention also relates to the construction of a chimeric gene encoding all or a portion of the glycolysis or respiration protein, in sense or antisense orientation, wherein expression of the chimeric gene results in production of altered levels of the glycolysis or respiration protein in a transformed host cell.

9 Claims, 1 Drawing figures
Exemplary Claim Number: 1,5,7,9
Number of Drawing Sheets: 1

DRPR:
The nucleic acid fragments of the instant invention may be used to create transgenic plants in which the disclosed BCS1 or 6-phosphofructo 2-kinase/fructose 2,6-bisphosphatase proteins are present at higher or lower levels than normal or in cell types or developmental stages in which they are not normally found. This would have the effect of modulating respiration or **altering the level of carbon flux** in glycolysis in those cells.

DEPR:
A selectable marker gene which can be used to facilitate soybean transformation is a chimeric gene composed of the 35S promoter from Cauliflower Mosaic Virus (Odell et al.(1985) Nature 313:810-812), the hygromycin **phosphotransferase** gene from plasmid pJR225 (from E. coli; Gritz et al.(1983) Gene 25:179-188) and the 3' region of the nopaline synthase gene from the T-DNA of the Ti plasmid of Agrobacterium tumefaciens. The seed expression cassette comprising the phaseolin 5' region, the fragment encoding the glycolysis or respiration protein and the phaseolin 3' region can be isolated as a restriction fragment. This fragment can then be inserted into a unique restriction site of the vector carrying the marker gene.

US-CL-CURRENT: 435/232,530/350 ,536/23.1 ,536/23.2 ,536/23.7

US-PAT-NO: 6136576
DOCUMENT-IDENTIFIER: US 6136576 A
TITLE: Method for the recombinant production of 1,3-propanediol
DATE-ISSUED: October 24, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Diaz-Torres; Maria	San Mateo	CA	N/A	N/A
Dunn-Coleman; Nigel S	Los Gatos	CA	N/A	N/A
Chase; Matthew W.	Belmont	CA	N/A	N/A
Trimbur; Donald	Redwood City	CA	N/A	N/A

US-CL-CURRENT: 435/158,435/232 ,530/350 ,536/23.1 ,536/23.2 ,536/23.7
ABSTRACT:

The present invention provides an improved method for the production of 1,3-propanediol from a variety of carbon sources in an organism capable of 1,3-propanediol production and comprising DNA encoding protein X of a microorganismal dehydratase or protein X in combination with at least one of protein 1, protein 2 and protein 3, which proteins are comparable to those encoded by orfY, orfX and orfW, respectively from a microorganismal dha regulon. The protein X may be isolated from a diol dehydratase or a glycerol dehydratase. The present invention also provides host cells comprising protein X that are capable of increased production of 1,3-propanediol.

17 Claims, 27 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 27

DEPR:
E. coli strain ECL707 was transformed with cosmid K. pneumoniae DNA corresponding to one of pKP1, pKP2, pKP4 or the Supercos vector alone and named ECL707-pKP1, ECL707-pKP2, ECL707-pKP4, and ECL707-sc, respectively. ECL707 is defective in gipK, gld, and ptsD which encode the ATP-dependent glycerol kinase, NAD.sup.+ -linked glycerol dehydrogenase, and enzyme II for dihydroxyacetone of the phosphoenolpyruvate-dependent **phosphotransferase** system, respectively.

DEPL:
Mutations and transformations that affect carbon channeling. A variety of mutant organisms comprising variations in the 1,3-propanediol production pathway will be useful in the present invention. The introduction of a triosephosphate isomerase mutation (tpi-) into the microorganism is an example of the use of a mutation to improve the performance by carbon channeling. Alternatively, mutations which diminish the production of ethanol (adh) or lactate (ldh) will increase the availability of NADH for the production of 1,3-propanediol. Additional mutations in steps of glycolysis after glyceraldehyde-3-phosphate such as phosphoglycerate mutase (pgm) would be useful to **increase the flow of carbon** to the 1,3-propanediol production pathway. Mutations that effect glucose transport such as PTS which would prevent loss of PEP may also prove useful. Mutations which block alternate pathways for intermediates of the 1,3-propanediol production pathway such as the glycerol catabolic pathway (glp) would also be useful to the present invention. The mutation can be directed toward a structural gene so as to impair or improve the activity of an enzymatic activity or can be directed toward a regulatory gene so as to modulate the expression level of an enzymatic activity.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	3000	carbon near2 (flux or flow)	USPAT; US-PGPUB	2001/06/04 15:26
2	L2	150	1 near4 (modif$8 or alter$8 or increas$8)	USPAT; US-PGPUB	2001/06/04 15:27
3	L3	104	(phosphoenol adj pyruvate or pep or phosphoenolpyruvate or phospho adj enol adj pyruvate) near4 (suppl$4 or availab$8)	USPAT; US-PGPUB	2001/06/04 15:28
4	L4	2	2 and 3	USPAT; US-PGPUB	2001/06/04 15:29
5	L5	2505	phosphotransferase$1 or phospho adj transferase$1	USPAT; US-PGPUB	2001/06/04 15:28
6	L6	8	(2 or 3) and 5	USPAT; US-PGPUB	2001/06/04 15:29
7	L7	19	(2 or 3) same (aromatic or shikimate)	USPAT; US-PGPUB	2001/06/04 15:31

US-CL-CURRENT: 530/300,536/23.1

US-PAT-NO: 6228638
DOCUMENT-IDENTIFIER: US 6228638 B1
TITLE: Escherichia coli CSRB gene and RNA encoded thereby
DATE-ISSUED: May 8, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Romeo; Tony	Burlington	TX	N/A	N/A

US-CL-CURRENT: 435/320.1,530/300 ,536/23.1
ABSTRACT:

The invention includes the gene csrB, the RNA encoded thereby and methods of use thereof. csrB RNA binds to and antagonizes the ability of CsrA to down-regulate the production of certain metabolic products. This invention is also drawn to methods of using csrB polynucleotides, and combination of csrB polynucleotides and CsrA polypeptides and antibodies that bind to such combinations.

6 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

BSPR:

Further "metabolic engineering" can lead to even greater yields of desired amino acids or other products. In addition to being an amino acid precursor, PEP is a precursor of glucose via gluconeogenesis. Glucose is, in turn, a precursor of glycogen. Gluconeogenesis and glycogen synthesis are elevated in csrA mutants and would compete for the synthesis of **aromatic** amino acids. Therefore, in order to further **increase carbon flow** into the desired products (e.g., amino acids), engineering of gluconeogenesis, glycogen biosynthesis and possibly other pathways is desirable. A mutation in jbp, which encodes fructose-1,6-bisphosphatase, prevents gluconeogenesis from proceeding beyond the synthesis of fructose-1,6-bisphosphate. A mutation in glgC (ADP-glucose pyrophosphorylase) or glgA (glycogen synthase) further blocks residual glucose or glucose derivatives obtained from the media or generated within the cell from being used for glycogen synthesis. Each of these mutations is already known and can be introduced into a cell by methods known in the art. Further enhancement of the synthesis of a single **aromatic** amino acid can be achieved by introducing mutations which block the synthesis of other amino acids.

US-CL-CURRENT: 435/232,435/252.3 ,435/320.1

US-PAT-NO: 6210937
DOCUMENT-IDENTIFIER: US 6210937 B1
TITLE: Development of genetically engineered bacteria for production of selected aromatic compounds
DATE-ISSUED: April 3, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ward; Thomas E.	Idaho Falls	ID	N/A	N/A
Watkins; Carolyn S.	Idaho Falls	ID	N/A	N/A
Bulmer; Deborah K.	Henderson	NV	N/A	N/A
Johnson; Bruce F.	Scotia	NY	N/A	N/A
Amaratunga; Mohan	Clifton Park	NY	N/A	N/A

US-CL-CURRENT: 435/146,435/232 ,435/252.3 ,435/320.1
ABSTRACT:

The cloning and expression of genes in the common aromatic pathway of E. coli are described. A compound for which chorismate, the final product of the common aromatic pathway, is an anabolic intermediate can be produced by cloning and expressing selected genes of the common aromatic pathway and the genes coding for enzymes necessary to convert chorismate to the selected compound. Plasmids carrying selected genes of the common aromatic pathway are also described.

14 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

BSPR:
Efficient and cost-effective biosynthetic production of chorismate and its biosynthetic derivatives require that carbon sources such as glucose, lactose, galactose, and other sugars be converted to the selected product in high percentage yields. Accordingly, it is valuable from the standpoint of industrial biosynthetic production of **aromatic** compounds or other biosynthetic derivatives of chorismate to **increase the flux of carbon** sources into and through the common **aromatic** pathway, thereby enhancing biosynthesis of chorismate and its derivatives.

DEPR:
In preferred embodiments, the present invention is a method for **increasing carbon flow** into the common **aromatic** pathway of a host cell and thence to the selected **aromatic** compound. **Increasing carbon flow** requires the step of transforming the host cell with recombinant DNA containing selected genes such that the respective gene products are expressed at enhanced levels relative to wild type cells.

ORPL:
G. Gosset et al., "A Direct Comparison of Approches For **Increasing Carbon Flow to Aromatic** Biosynthesis in Escherichia coli" J. Indust. Microbiol. 17(1):47-52, Jul. 1996.

US-CL-CURRENT: 435/195,435/252.3 ,435/252.33 ,435/320.1 ,435/41 ,435/440 ,435/455 ,435/69.1 ,536/23.1 ,536/23.2 ,536/23.7

US-PAT-NO: 6190892
DOCUMENT-IDENTIFIER: US 6190892 B1
TITLE: Microbial production of indigo
DATE-ISSUED: February 20, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Weyler; Walter	San Francisco	CA	N/A	N/A
Dodge; Timothy C.	Rochester	NY	N/A	N/A
Lauff; John J.	Rochester	NY	N/A	N/A
Wendt; Dan J.	San Mateo	CA	N/A	N/A

US-CL-CURRENT: 435/170,435/195 ,435/252.3 ,435/252.33 ,435/320.1 ,435/41 ,435/440 ,435/455 ,435/69.1 ,536/23.1 ,536/23.2 ,536/23.7

ABSTRACT:
There is provided an improved process for the biosynthetic production of indigo, the improvement comprising removing unwanted by-products such as isatin or indirubin from the broth in which such indigo is produced. Isatin can be removed by enzymatic activity using an isatin-removing enzyme such as an isatin hydrolase, or by other techniques such as process parameters (elevated temperature, pH), or by contacting the broth containing the isatin with appropriate adsorption compounds/compositions such as carbon or appropriate resins. Since isatin is the precursor of indirubin, the indirubin levels are decreased as a result of isatin removal.
20 Claims, 11 Drawing figures
Exemplary Claim Number: 6
Number of Drawing Sheets: 13

BSPR:
Tryptophan pathway genes useful in securing biosynthetic indole accumulation include a trp operon, isolated from a microorganism as a purified DNA molecule that encodes an enzymatic pathway capable of directing the biosynthesis of L-tryptophan from chorismic acid. (A. J. Pittard (1987) Biosynthesis of **Aromatic** Amino Acids in Escherichia coli and Salmonella typhimurium, F. C. Neidhardt, ed., American Society for Microbiology, publisher, pp. 368-394.) Indole accumulation is enabled by modification of one or more of the pathway's structural elements and/or regulatory regions. This modified trp operon may then be introduced into a suitable host such as a microorganism, plant tissue culture system or other suitable expression system. It should be noted that the term "indole accumulation" does not necessarily indicate that indole actually accumulates intracellularly. Instead, this term can indicate that there is an **increased flux of carbon** to indole and indole is made available as a substrate for intracellular catalytic reactions such as indoxyl formation and other than the formation of L-tryptophan. In the context of this invention, the "accumulated" indole may be consumed in the conversion of indole to indoxyl by an oxygenase such as the **aromatic** dioxygenase NDO, or an **aromatic** monooxygenase such as TMO, or it may actually build up intracellularly and extracellularly, as would be the case when the desired end product is indole or one of its derivatives.